REMARKS

Claims 1-45 currently are pending. Claims 46-48 were previously canceled. Claims 1 and 45 are amended herein.

Claim 1-45 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

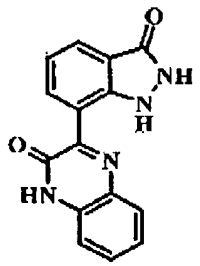
Claims 1 and 45 were amended to specifically recite pyrrolidin-1-yl, piperidin-1-yl, morpholin-1-yl and piperazin-1-yl substitution on the said rings rather then incorporating the above ring structures into possible variations of the dialkylamino. This amendment describes instantly claimed compounds in an alternative form and therefore does not introduce new matter. Claims 1 and 45 were also amended to replace "isomers" with –stereoisomers-- as suggested in the Office Action.

Claims 1-6, 15-17, 25-28, 36, 37 and 45 are provisionally rejected on the ground of nonstatutory obvious-type double patenting as being unpatentable over claims 1, 2, 14 and 15 of copending Application No. 10/916,073.

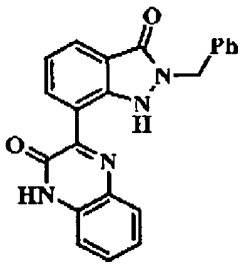
As neither the current application nor the co-pending '073 application has been allowed to date and this is the first to receive an examination on the merits, Applicants believe no action is required in regard to this objection. Should this application be allowed prior to the co-pending application the provisional rejection will be withdrawn. If necessary applicants will file a terminal disclaimer when other issues have been resolved.

Claims 1 and 45 are rejected under 35 U.S.C. §102(a) as being anticipated by Hayama et al {WO 2002/002550}. Since the WO is in a non-English language, the U.S. equivalent, U.S. 6,914,062 will be referred to hereinafter.

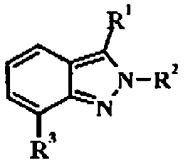
The Office Action asserts that, for example, the instant claimed invention embrace Example 24 in column 51; Example 27 in column 52, etc. of the Hayama *et al.* application



Example 24



Example 27



I

Hayama US 6,914,062

The compounds disclosed by Hayama differ from those in the instant application. Both cited compounds in the reference (Example 24 and 27) have an oxo substituent to the C3 position (equivalent to R^1 = OH in the instant claims if the other tautomer is drawn). However, the instant claims limit R^1 to "-NR^aR^b, -$CR^cR^dR^e$, CO_2R^a, or -$C(O)NR^aR^b$; or R^1 is hydrogen, cycloalkenyl, aryl, or heteroaryl" (the optional substituents listed in the claim are not reproduced). Applicants suggest it is impossible to arrive at compounds in the instant claims from the most general formulae **I** (column 4), **I-a** (column 17), **I-p1** (column 20) or **I-p2** (column 21) in the Hayama reference.

Using the broadest generic formula (**I**) (col. 4), the only way to arrive at an indazole is let W_n be $(CH_2)_n$ and n be zero. Z and Y must both be N since Z can not be N (Z can be NCOR, however this does not encompass the instantly claimed compounds. The only remaining variable in the five-membered ring is Z which must be CO, SO, SO_2 or NCOR. Only CO produces an 1,2-dihydro-indazol-3-one ring but the oxo substituent at C3 (or hydroxy depending which equivalent tautomeric form is drawn) does not fall within the scope of the instant claims.

Applicants respectively suggest that there is no anticipation by Hayama and request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(a) or Applicants request a specific demonstration of how the substituents in generic formula disclosed by Hayama can be used to arrive at the instant claimed compounds.

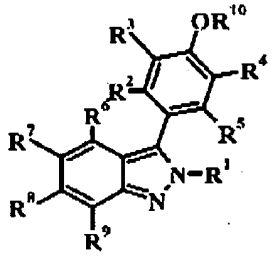
Claims 1, 2 and 45 are rejected under 35 U.S.C. §102(b) as being anticipation by Saito *et al.* (Heterocycles (1992), 34(1), pages 129-134.

Saito discloses a single species which is used as an intermediate. Claim 1 and 45 have been amended to exclude a compound with R^1 = hydrogen. The amended claims are no longer anticipated by Saito *et al.*

Since claim 2 is dependent on claim 1, the compounds of claim 2 also are no longer anticipated by Saito *et al.* Withdrawal of the rejected over Saito is respectfully requested.

Claims 1, 2 and 45 are rejected under 35 U.S.C. §102(e) as being anticipated by Steffan *et al.* {US 2004/0167127}

The compounds disclosed by Steffan *et al.* are characterized by formula II (page 1 of the '127 application) The compounds require the aryl substituent at C3 contain an OR^{10} substitutent at the 4 position of the aryl substituent where R^{10} is defined as hydrogen, COR^{11} (*i.e.*, an ester), $-CONHR^{11}$ (*i.e.*, a carbamate or urethane), $-P(=O)(OH)OR^{11}$, or $-CO(CH_2)_nCH(NHR^{12})COR^{11}$. The second compound cited in the Office Action from Example 110 corresponds to formula II where R^{10} is hydrogen. Claim 1 of the present application does include optional hydroxy substitution on the phenyl substitutent at R^1 of formula I, therefore there is no anticipation by the second compound in Example 110 of the Steffan reference.



(II)

The first compound cited in Example 110 has a methoxy substitutent (R^{10} = methyl) which is a synthetic intermediate which is demethylated to provide a compound within the scope of the claims. A CAS STN search of exemplified compounds revealed although methoxy substituted phenyl substituents are common synthetic intermediates leading to the claimed phenols disclosed in the '127 application, the compound cited in the Office Action is the only exemplified compound which is substituted by an aryl or heteroaryl moiety at the position corresponding to R^3 of the compounds claimed in the instant application. All the remaining examples in the '127 application have substitution other than aryl or heteroaryl at R^9.

The Steffan reference is limited to unsubstituted phenyl substituents as R^9 of the Steffan generic formula. Neither the claims nor the specification disclose substituted phenyl and the definition of "aryl" in paragraph [0011] does not disclose substituted phenyl. Steffan does disclose compounds with a 4-methoxy phenyl substituent at C3 optionally further substituted by one or more C_{1-6} alkoxy groups that are synthetic intermediates (see paragraph [0049] and the definition of R^2-R^5 in paragraph [0010]. Claims 1 and 45 have

been amended to include the proviso that "R^1 can not be a 4-methoxyphenyl substituent when R^3 is unsubtituted phenyl" which avoids any anticipation by the Steffan reference.

> When the compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g., select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated. *Ex parte A*, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990). If one of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula, the compound is anticipated. One of ordinary skill in the art must be able to draw the structural formula or write the name of each of the compounds included in the generic formula before any of the compounds can be "at once envisaged." One may look to the preferred embodiments to determine which compounds can be anticipated. *In re Petering*, 301 F.2d 676, 133 USPQ 275 (CCPA 1962).

[MPEP §2131.02]

In the present case only one compound found in example 110 anticipates compounds disclosed in the instant invention and that compound has now been eliminated from the claims by addition of a proviso. The remaining 223 examples disclosed do not contain both alkoxyphenyl substitution at C3 on the indazole and aryl or heteroaryl substituent at C-7 of the indazole. Applicants assert that there is nothing which would lead one from the large generic disclosure in the '127 application, which includes alkoxy substituted phenyl indazoles utilized as synthetic intermediates for the production of estrogen receptor ligands outside the scope of the instant claims, to the instant claimed CRF antagonists with the exception of the single disclosed species which has now been eliminated from the claims 1 and 45 by the proviso.

Claims 1-6, 15-17, 25-28, 36, 37 and 43-45 are rejected under 35 U.S.C. §103(a) as being unpatentable over Bhagwat *et al* {U.S. Pat. No. 6,897,231} and Hayama *et al.* {WO 2002/002550} each taken alone. Since the WO is in a non-English language the US equivalent, U.S. 6,914,062, will be referred to hereinafter.

The Office Action asserts that Bhagwat *et al.* teach in U. S. pat. No 6,897,231, which is the equivalent of WO 2002/002550, structurally similar compounds which are positional isomers of the instantly claimed compounds. The Office Action further asserts that "[t]he motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g. anti-cancer).

Bhagwat teaches compounds which differ from the instantly claimed compounds. Bhagwat discloses compounds requiring substitution at the C5-position whereas the C7-position is unsubstituted. Furthermore, perusal of the examples quickly suggests the C7 substitutent typically contains a nitrogen containing group capable of participating in a hydrogen bond which is not disclosed in the instantly claimed compounds. In contrast the instantly claimed compounds have a hydrogen at the C5-position and aryl or heteroaryl substitutent at the C7 position. C3 substituents taught by Bhagwat contain an aryl, heteroaryl or heterocycle

either directed linked to the indazole or connected through an "A" group (see col. 6, lines 24-29 of the '231 patent) whereas the instantly claimed compounds contain many examples which lack a aryl, heteroaryl or heterocycle (compare, *e.g.* examples 1-11 of the instantly claimed compounds). In addition Bhagwat discloses compounds which are exclusively 1H-indazoles (col. 4, line 20) whereas the instant compounds are 2H-indazoles. The common thread throughout the Bhagwat compounds is the fused 1H-pyrazin-2-one ring which typically is a 1H-quinoxalin-2-one which is optionally substituted. To attempt to infer some role for the 1,2-dihydro-indazol-3-one moiety which appears only sporadically among the disclosed compounds and then extrapolate to a significantly different compound series with a distinctly different activity is unsound.

Bhagwat teaches compounds which are useful as protein kinase inhibitors, specifically JNK kinase. JNK is a cytosolic intracellular protein important in signal transduction (col. 1-4). The instantly claimed compounds are antagonists of the CRF receptor which is a seven-transmembrane G-protein linked receptor. Thus the biomacromolecular targets for the two groups of compounds are entirely unrelated. JNK kinase is on the signal pathway initiated by pro-inflammatory cytokines and antagonists are claimed to be useful for the treatment of inflammatory, autoimmune and neoplastic diseases (col. 2-4 of the '231 patent). The instantly claimed compounds modulate CRF activity which is disclosed as useful for neuropsychiatric and stress-related disorders (p. 1 of the instant application). Any asserted relationship between the therapeutic uses for the two compounds is, at best, tenuous.

> The presumption of obviousness based on a reference disclosing structurally similar compounds may be overcome where there is evidence showing there is no reasonable expectation of similar properties in structurally similar compounds. *In re May*, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978) (appellant produced sufficient evidence to establish a substantial degree of unpredictability in the pertinent art area, and thereby rebutted the presumption that structurally similar compounds have similar properties); *In re Schechter*, 205 F.2d 185, 98 USPQ 144 (CCPA 1953). See also *Ex parte Blattner*, 2 USPQ2d 2047 (Bd. Pat. App. & Inter. 1987) (Claims directed to compounds containing a 7-membered ring were rejected as *prima facie* obvious over a reference which taught 5- and 6-membered ring homologs of the claimed compounds. The Board reversed the rejection because the prior art taught that the compounds containing a 5-membered ring possessed the opposite utility of the compounds containing the 6-membered ring, undermining the examiner's asserted *prima facie* case arising from an expectation of similar results in the claimed compounds which contain a 7-membered ring.).

[MPEP §2144.09]

The instant compounds have utility unrelated to that taught by Bhagwat. The structures of the compounds disclosed by Bhagwat are sufficiently different from the instantly claimed compounds that there would be no

expectation that the compounds would have similar biological activity much less activity against two entirely different classes of receptors and useful for entirely different indications.

The Office action asserts that Hayama *et al.* (columns 17-19, 44 and 45; and especially Example 24 in column 51 and Example 27 in column 52) teach indazole compounds which are either structurally the same as (see 102 rejection) or structurally similar to the instant claimed compounds. The instant claimed compounds are assert to be generically described in Hayama.

As argued above in regard to the 35 U.S.C. §102(b) rejection, the assertion that instantly claimed compounds are generically described by Hayama *et al.* is simply incorrect. Furthermore the Hayama disclosure describes compounds which inhibit Cdk 4 and/or Cdk 6 and are disclosed to be useful anticancer agents. Cdk (Cyclin-dependent kinase) like Jun (*supra*) is a intracellular kinase intricately connected to regulation of the cell cycle and is completely unrelated to CRF. Furthermore the indications disclosed are again entirely unrelated.

In order to establish *prima facie* obviousness, three basic criteria must be met. First, the prior art must provide one of ordinary skill in the art with a suggestion or motivation to modify or combine the teachings of the references relied upon by the PTO to arrive at the claimed invention. The suggestion or motivation to combine generally arises in the references, but may also be inferred from the nature of the problem or the knowledge of those of ordinary skill in the art. *WMS Gaming Inc. v. International Game Technology*, 51 USPQ2d 1385, 1397 (Fed. Cir. 1999). The mere fact that references could be modified or combined does not render the resultant modification or combination obvious unless the prior art also suggests the desirability of the modification or combination. *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990); MPEP § 2143.01. Second, the prior art must provide one of ordinary skill in the art with a reasonable expectation of success. Thus, in light of the teachings of the prior art, the skilled artisan must have a reasonable expectation that the modification or combination suggested by the Examiner would succeed. *In re Dow*, 5 USPQ2d 1529, 1531-32 (Fed. Cir. 1988). Third, either alone or in combination, the prior art must teach or suggest each and every limitation of the rejected claims. *In re Gartside*, 53 USPQ2d 1769(Fed. Cir. 2000). The teaching or suggestion to make the claimed invention, as well as the reasonable expectation of success, must come from the prior art and not Applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). If any one of these criteria are not met, *prima facie* obviousness is not established, and Applicants are not required to show new or unanticipated results. *In re Grabiak*, 226 USPQ 870 (Fed. Cir. 1985).

The Office Action fails to establish any one of the three required criteria to establish *prima facie* obviousness. There is no suggestion in the prior art references that any indazoles, much less the instantly claimed 2H-

indazole compounds would antagonize CRF or be useful for treating anxiety, depression or psychiatric disorders. Nothing in the prior art references would motivate one skilled in the art to prepare modify compounds in the disclosures in a manner which would lead to the instantly claimed compounds. There is no expectation of success. Neither of the prior art references teaches 2-substituted 2H-indazoles which are a feature of the instantly claimed compounds. None of the references teaches compound which interact with G-protein linked receptors or which would be useful to treat psychiatric or stress related disorders.

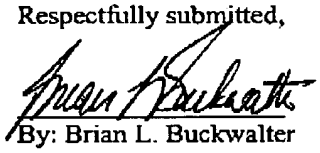
Reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

CONCLUSIONS

Applicants assert that the amended claims are no longer anticipated by any of the cited references in the Office Action and the Office Action fails to meet the requirements for a *prima facie* case of obviousness. Reconsideration and withdrawal of the rejections and allowance of the amended claims is respectfully requested. Applicants have included a petition for a 1 month extension of time to reply to the Office Action. The USPTO is authorized to charge deposit account number 18-1700 the requisite fee. No other fees are believed to be required, but in the event a fee is required, the Examiner is authorized to charge our deposit account.

If the Examiner believes a telephone conference will expedite the prosecution of this application, the Examiner is invited to contact the undersigned at the number indicated below.

Respectfully submitted,



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HETEROCYCLES, Vol. 34, No. 1, 1992

ELECTROCHEMICAL FORMATION OF INDAZOLES FROM TROPONE TOSYLHYDRAZONES: ELECTROCHEMICAL OXIDATIONS OF SODIUM SALTS OF TOSYLHYDRAZONES OF TROPONE AND 2-PHENYLTROPONE

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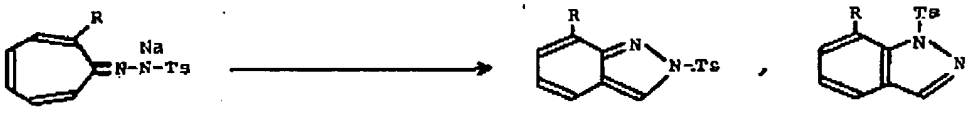
Abstract —— Electrochemical oxidations of the sodium salts of tropone and 2-phenyltropone tosylhydrazones afforded 2-tosyl-2H-indazole and 1-tosyl-7-phenyl-1H-indazole, respectively. Tho reactions proceeded through the cyclizations of the corresponding hydrazyl radicals generated by electrochemical one electron oxidations of the hydrazone anions.

Much attention has been paid to electrochemical reactions of organic compounds not only from the viewpoint of synthetic utilities but also from elucidation of the reaction mechanisms.[1] The electrochemical reactions of nitrogen atom-containing compounds such as amines, imines, and hydroxylamines have been revealed to proceed mainly through one electron oxidation of the lone pair electrons on the nitrogen atoms.[2] There is, however, a paucity on the papers dealing with the electrochemical reactions of hydrazones. And it is hard to find any document except for the electrochemical dimerization through cation radicals formed by one electron oxidation.[3]

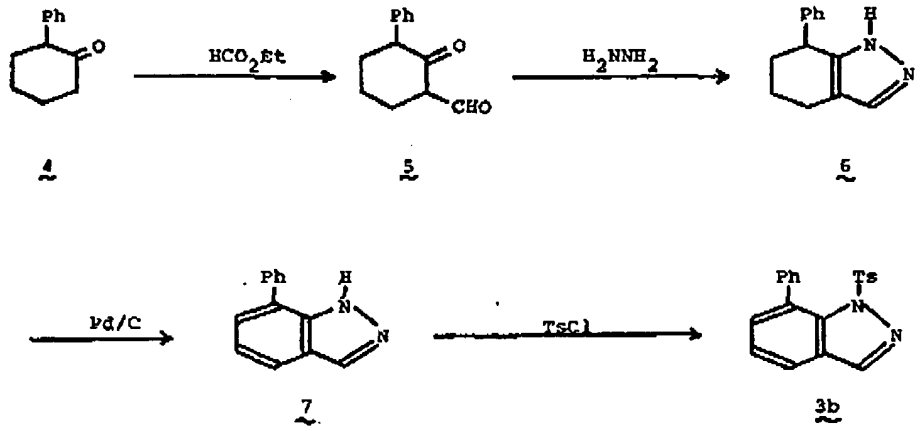


1a: R=H
b: R=Ph

2 3

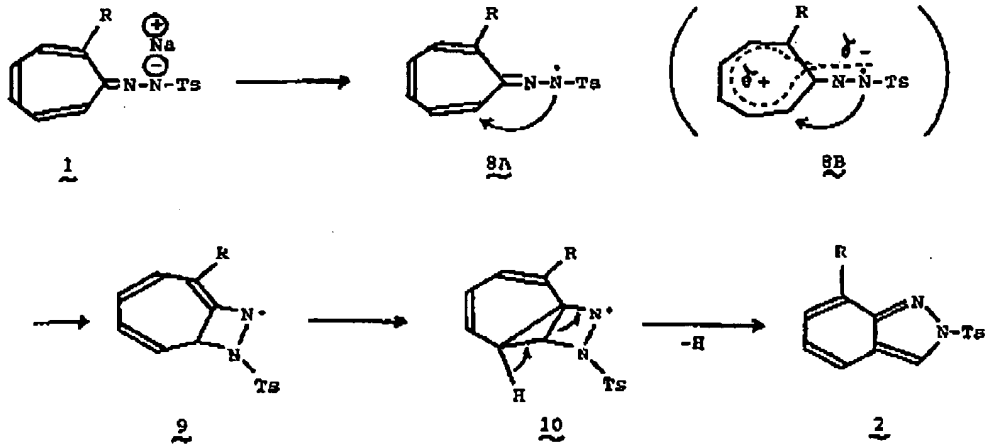
Sodium salts of tropone tosylhydrazones (1) are known to generate cyclic carbenes (cycloheptatrienylidene) or cyclic allenes (cycloheptatetraene) and their thermal and photochemical reactivities have been elucidated in very detail.[4, 5] However, we are unaware of any work concerning the electrochemical reactivities of these hydrazones. As a part of a series of our researches on the reactivities of tosylhydrazones,[5-7] we investigated into the electrochemical oxidation reactions of the sodium salts of tropone tosylhydrazones (1) affording indazole derivatives. The results are reported herein.

A solution of tropone tosylhydrazone sodium salt (1a) in anhydrous N,N-dimethylformamide (DMF) was electrolyzed in the presence of tetrabutylammonium perchrolate as a supporting electrolyte with a platinum wire as a cathode, a platinum gauze as an anode, and a silver wire as a reference electrode at + 0.6 V at room temperature under a nitrogen stream. After evaporation of the solvent under a reduced pressure, the reaction mixture was chromatographed on silica gel to give 2-tosyl-2H-indazole (2a) in 28% yield. A similar reaction on 2-phenyltropone tosylhydrazone sodium salt (1b)[8] at +1.1 V afforded 1-tosyl-7-phenyl-1H-indazole (3b) in 17% yield.[9]



The structure of 2a was determined by the coincidence of the spectral properties and melting point to those of the authentic sample.[7] The structure of 3b was also determined by the coincidence of it's melting point and spectral properties to those of the authentic sample, which was synthesized from 2-phenylcyclohexanone (4) via 2-oxo-3-phenylcyclohexanonecarbaldehyde (5), 4,5,6,7-tetrahydro-7-phenyl-1H-indazole (6), and 7-phenyl-1H-indazole (7).[10]

The formation of 2 can be speculated to proceed as follows. Electrochemical one electron oxidation of 1 forms a hydrazyl radical (8), which cyclized to give a cycloheptatriene-type intermediate (9). The ionic form (8B) is thought to contribute to this cyclization process through an interaction between the counter electric charges. A norcaradiene-type valence tautomer (10) opens its cyclopropane ring forming 2.[7,11]



ACKNOWLEDGEMENT

The authors are indebted to Professors Kaname Ito and Shoichiro Ikeda of Nagoya Institute of Technology for their fruitful suggestions.

EXPERIMENTAL

The anode was a platinum gauze of a size of 5 cm depth and 12 cm width which was separated from the cathode compartment by means of a medium-porosity sintered glass frit. The cathode was a platinum wire and the reference electrode was a silver wire. The controlled potential power was supplied from a Yanaco Potentio/Garvanostatic Electrolyser VE-9 apparatus. Melting points were recorded on a Yanagimoto Micro Melting Point Apparatus and were uncorrected. Nmr spectra were measured with Varian XL 200 spectrometer with tetramethylsilane as an internal standard. Ir and uv spectra were measured with JASCO FT/IR 5300 and Hitachi 200-10 spectrophotometers, respectively. Ms spectra were measured with a Hitachi M-2000S spectrometer.

Electrolysis of 1a. A solution of 1a (590 mg, 2 mmol), tetrabutylammonium perchlorate (6840 mg, 20 mmol) in DMF (200 ml) was electrolyzed under a nitrogen stream at room temperayure at +0.6 V. After removing the solvent by distillation under a reduced pressure (62°C, 5 mmHg) the resulting residue was chromatographed on silica gel to give colorless crystals (2a) (150 mg, 28%, mp 140°C, lit.,[7] mp 140° C, hexane-ethyl acetate (8:2)) and red crystals of tropone tosylhydrazone (110 mg, 13%, hexane-ethyl acetate (1:1)).

Electrolysis of 1b. A solution of 1b (780 mg, 2 mmol), tetrabutylammonium perchlorate (6840 mg, 20 mmol) in DMF (200 ml) was electrolyzed at +1.05 V under the same reaction conditions as above to give brown crystals (3b) (130 mg, 17%) from elution with hexane-ethyl acetate (8:2) on silica-gel chromatography.

3b: mp 94-96°C. Hrms: m/z 348.0944. Calcd for $C_{20}H_{16}N_2O_2S$: m/z 348.0943. Ms m/z (rel intensity): 348 (M^+, 100), 284 (63). Uv (MeOH): 239 nm (log ε, 4.33), 273 (3.96), 276 (3.98), 293 (3.86), 330 (3.86). Ir (KBr): 3030, 2950, 1385, 1192, 1059 cm^{-1}. ^1H Nmr ($CDCl_3$) δ 2.40 (s, 3H), 7.15-7.64 (m, 8H), 7.93-8.04 (m, 4H), 8.70 (s, 1H). ^{13}C Nmr ($CDCl_3$) δ 21.7, 120.2, 122.6, 124.3, 124.6, 127.1, 127.8, 128.4, 128.7, 128.8, 130.0, 130.1, 131.6, 133.6, 137.3, 146.3.

Synthesis of 3b. To a solution of 4 (1740 mg, 10 mmol) and ethyl formate (1110 mg, 15 mmol) in anhydrous ether (40 ml) were added sodium metal (230 mg, 10 mmol) and one drop of ethanol. After stirring at room temperature for 24 h ethanol (1 ml) was added and the mixture was further stirred for 1 h. The reaction mixture was washed with water, and dried over anhydrous sodium sulfate. Evaporation of the solvent and separation of the residue with chromatography (silica gel, ether) afforded 2-oxo-3-phenylcyclohexanonecarbaldehyde (5) as a yellow oil (1790 mg, 89%).

5: Hrms: m/z 202.0980. Calcd for $C_{13}H_{14}O_2$: m/z 202.0992. Ms m/z (rel intensity): 202 (M^+, 100), 174 (56), 146 (35). Ir (oil): 3030, 2940, 1712 cm^{-1}. ^1H Nmr ($CDCl_3$) δ 1.33-2.22 (m, 5H), 2.38-2.55 (m, 2H), 3.57-3.73 (m, 1H), 7.03-7.41 (m, 5H), 8.85 (s, 1H). ^{13}C Nmr ($CDCl_3$) δ 20.4, 23.2, 31.1, 47.2, 109.5, 126.5, 128.1, 128.2, 141.5, 182.9, 189.2.

To a solution of 5 (1410 mg, 7 mmol) in methanol (10 ml) was added hydratine hydrate (350 mg, 7 mmol) dropwisely and the mixture was stirred at room temperature for 30 min. After evaporation of the solvent the residue was chromatographed (silica gel, hexane-ethyl acetate (3:2)) to afford colorless crystals of 4,5,6,7-tetrahydro-7-phenyl-1H-indazole (6) (1260 mg, 91%).

6: mp 115-116°C. Hrms: m/z 198.1156. Calcd for $C_{13}H_{14}N_2$: m/z 198.1156. Ms m/z (rel intensity): 198 (M^+, 100), 169 (54), 143 (18). Ir (KBr): 3159, 2928, 1493 cm^{-1}. ^1H Nmr ($CDCl_3$) δ 1.62-2.32 (m, 5H), 2.50-2.68 (m, 2H), 3.88-4.07 (m, 1H), 7.04-7.38 (m, 6H). ^{13}C Nmr ($CDCl_3$) δ 20.4, 21.9, 33.9, 40.0, 115.9, 120.4, 120.4, 127.9, 128.4, 133.4, 143.4, 144.3.

A mixture of 6 (200 mg) and palladium-carbon (5%, 85 mg) in decalin (2.5 ml) was refluxed for 24 h. The reaction mixture was chromatographed (silica gel, hexane-ethyl acetate (3:2)) to give colorless crystals (7) (140 mg, 70%).

7: mp: 151-153°C. Hrms: m/z 194.0833. Calcd for $C_{13}H_{10}N_2$: m/z 194.0843. Ms m/z (rel intensity): 194 (M^+, 100), 167 (30). Uv (MeOH): 266 nm (log ε, 3.98), 301 (4.06). Ir (KBr): 3258, 3030, 2950, 1429 cm^{-1}. ^1H Nmr ($CDCl_3$) δ 7.23-7.78 (m, 9H), 8.08 (s, 1H). ^{13}C Nmr ($CDCl_3$) δ 119.9, 121.5, 124.6, 126.0, 127.7, 127.8, 127.9, 129.2, 135.3, 138.0, 138.8.

A solution of 7 (17 mg, 0.09 mmol) and tosyl chloride (170 mg, 0.9 mmol) in pyridine (5 ml) was heated at 118°C for 2.5 h. The mixture was diluted with benzene, washed with water, and dried over anhydrous sodium sulfate. After filtration the solvent was removed on a rotary evaporator and the residue was chromatographed (silica gel, hexane-ethyl acetate (4:1)) to give brown crystals (3b) (14 mg, 46%).

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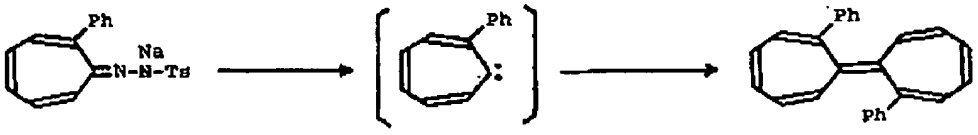

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Received, 17th October, 1991